PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of

Eugene A. Woltering *et al.*

Serial No. 09/866,296

Filing Date May 25, 2001

Group 1651

Examiner Afremova, Vera

For: Three-Dimensional *Ex Vivo* Angiogenesis System (File No. 98M06.1 Woltering)

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF EUGENE A. WOLTERING

STATE OF LOUISIANA

PARISH OF ORLEANS

Eugene A. Woltering declares as follows:

CERTIFICATE

I hereby certify that this Declaration of Eugene A. Woltering is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on April 21, 2004.

John H. Runnels
Registration No. 33,451
April 21, 2004

1.

I, Eugene A. Woltering, am one of the inventors of the above-identified patent application. I make this Declaration in support of that application.

Collagen-Containing Matrix

2.

I understand that the Patent and Trademark Office has questioned whether the written disclosure of the patent application would suffice to enable a person of ordinary skill in the art to practice the inventions as claimed, where the matrix contains collagen. The experiments described in Paragraphs 3 - 6 below were recently conducted in my laboratory under my direction to address this question.

3.

The experiments were conducted essentially as described in the specification of this application, page 25, line 1 through page 26, line 15, except as mentioned otherwise. In particular, in lieu of the fibrin / thrombin clot matrix described on pages 25 and 26 of the specification, 100 µL of ECM gel from Sigma-Aldrich was used to form a gel matrix. All other aspects of the tissue culture medium were essentially the same as described in the specification. Comparison experiments were also run simultaneously in a fibrin / thrombin clot system as otherwise described in the specification.

4.

The composition of ECM (extracellular matrix) gel, derived from Engelbreth-Holm-Swarm murine sarcoma, is similar to that of Matrigel™ basement membrane matrix.

According to the website of Sigma-Aldrich (from whom our laboratory ordered the ECM gel), "ECM gel is composed primarily of laminin, collagen type IV, heparan sulfate proteoglycan and entactin." Thus a matrix formed from ECM gel is a collagen-based matrix.

5.

Samples from a fresh ovarian carcinoma taken from a patient in Oregon were tested in both a fibrin/thrombin clot system, and in a collagen-based system formed with ECM gel. In the fibrin/thrombin clot system, 35 wells were plated. Of those 35 wells, 22 (62.9%) initiated an angiogenic response. In the ECM system, 10 wells were plated. Two of those wells were lost for evaluation, and 8 of the ECM wells were evaluated. One well developed an angiogenic response (12.5%). The angiogenic response in that ECM-containing well developed during the first 11 days. However, upon reevaluation on day 18, angiogenic vessels were no longer observed. Thus angiogenesis arising from a tumor fragment was observed in both fibrin- and collagen-based matrices, although the collagen-based system was less efficient.

6.

These experimental data support the conclusion that collagen-based matrices may be successfully used in practicing the claimed inventions. The fibrin/thrombin system currently remains our preferred system.

The Gulec *et al.* Paper

7.

I was one of the nine co-authors of S. Gulec *et al.*, "Antitumor and Antiangiogenic Effects of Somatostatin Receptor-Targeted *in Situ* Radiation with ^{111}In-DTPA-JIC 2DL," *J. Surg. Res.*, vol. 97, pp. 131-137 (2001) (the "Paper"). I understand that the Paper has been cited against the above application. I understand that the Paper was published in May 2001. The "official" publication date appearing on the journal issue is May 15, 2001. Recent communications with the journal's editorial staff suggested that the actual publication date for this issue was instead May 7, 2001. Both of these dates were nearly contemporaneous with, but slightly earlier than, the May 25, 2001 filing date of the present patent application. In particular, both of these dates were well within one year of the filing date of the present application. I further note that both of these dates were after the May 30, 2000 priority date that has been claimed under 35 U.S.C. § 119(e).

8.

Seza A. Gulec and I are the only inventors of the inventions claimed in this patent application, and of any aspects of the claimed inventions that are described in the cited Paper.

9.

The nine co-authors of the paper were the two inventors of the present application, and seven additional authors. The considerations in listing authors on a scholarly paper are different from the strict considerations that I am informed are involved in identifying the inventor or inventors in a United States patent application. The seven co-authors each

learned of the claimed inventions from me or my co-inventor Dr. Gulec, but none of them is an inventor of any of the claimed inventions.

10.

More specifically, the principal reasons for naming the other seven as co-authors on the Paper were the following:

(a) George J. Drouant and **(b)** Joseph Fuselier radiolabelled the somatostatin analogs whose use is described in the Paper.

(c) Catherine T. Anthony supervised the performance of the experiments described in the Paper, under the general direction of Dr. Gulec and me.

(d) James Heneghan was responsible for the care of the nude mice.

(e) Joseph B. DelCarpio conducted the histology and microscopy described in the Paper, under the general direction of Dr. Gulec and me.

(f) David H. Coy and **(g)** William A. Murphy both contributed to the conception of the somatostatin analogs whose use is described in the Paper, and they also supplied the samples of the somatostatin analogs that were used in the experiments described in the Paper.

Conclusion

11.

All statements made in this Declaration of my own knowledge are true. All statements made in this Declaration on information and belief are believed to be true. These statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the above-identified patent application or any patent issuing from that application.

Eugene A. Woltering

April 19th, 2004